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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P200201386WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/DK 03/00654	International filing date *(day/month/year)* 02.10.2003	Priority date *(day/month/year)* 02.10.2002
International Patent Classification (IPC) or both national classification and IPC A61K39/39		
Applicant NORDIC VACCINE TECHNOLOGY A/S et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 12 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26.04.2004	04.01.2005
Name and mailing address of the International preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Herrero, M Telephone No. +49 89 2399-8542

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/DK 03/00654

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1, 2, 5-29, 32-53	as originally filed
3, 3a, 4, 30, 31	received on 20.12.2004 with letter of 17.12.2004

Claims, Numbers

1-37	received on 20.12.2004 with letter of 17.12.2004

Drawings, Sheets

1/13-13/13	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

   see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 35-37 with respect to industrial applicability

   because:

   ☒ the said international application, or the said claims Nos. 35-37 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-37
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1, 2, 4-27(part), 28, 29-37(part)
	No:	Claims	3, 4-27(part), 29-37(part)
Industrial applicability (IA)	Yes:	Claims	1-34
	No:	Claims	

2. Citations and explanations

see separate sheet

SECTION I

6. Additional observations

6.1 The amendments to the description and the newly filed Claims 1-37 submitted with the letter dated 17.12.04 have their basis in the originally filed application, and therefore do not contravene Art. 34(2)(b) PCT.

6.2 The newly filed Claims 1-37 include two claims numerated as "Claim 4". For the purposes of the present report the second Claim 4, which is directed to a "Construct" (i.e. consistent with the rest of the amended claims), has been taken into account.

Similarly, it has been considered that instead of referring to a "Composition" the newly filed dependent Claim 28 was meant to read "Construct".

SECTION III

Claims 35-37 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT (i.e. methods of treatment of the human or animal body by therapy). Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

SECTION V

2. CITATIONS AND EXPLANATIONS

2.1 In view of the priority documents pertaining to the present application, the document WO 02/080981 (publication date 17.10.02), cited in the International Search Report under the "P" category, is not to be regarded as state of the art according to Rule 64 (1) PCT, as the date of priority of 02.10.02 is validly claimed for the relevant parts of the application.

2.2 The following documents have been considered for the purposes of this report:

D1: WO 02/074325
D2: WO 99/11247
D3: WO 00/07621
D4: WO 99/43350

The document D4, which is cited in the application, was not cited in the international search report . A copy of the document has been provided to the Applicants.

2.3 Novelty and inventive step (Art. 33(2) and (3) PCT)

Present Claims 1-37 would appear to relate to subject-matter which is formally novel over the available prior art as required by Art. 32(2) PCT.

The counterarguments in reply to the objection under Art. 33(3) PCT raised in the written opinion of 19.10.04 put forward in the Applicants' letter dated 17.12.04, have been carefully considered. In this respect it is admissible that the present application provides an improved construct for transdermal delivery of an immunogen without invasive administration (e.g. without pre-treatment of the skin) which may be regarded as non-obviously derivable from the teachings of the available prior art (cf D1-D3). Said improved construct comprises a type of delivery system which is a complex possessing the characterizing features defined in present Claim 1, in combination with an occlusion vehicle, preferably in the form of an adherent vehicle (the said delivery system is denominated in the description as "PosIntro").

Hence, the constructs according to present Claims 1, 2, 4-27 (part), 28 and 32-34(part), which are characterized by comprising the particulate delivery system referred to above, appear to fulfill the inventive step requirements of Art. 33(3) PCT. A similar positive opinion with regard to Art. 33(3) PCT applies to the processes for the preparation of said constructs pursued in present Claims 29-31 and to the therapeutical applications of said constructs defined in present Claims 35-37.

Nevertheless, the broadly formulated construct embraced by independent Claim 3

does not rely on the type of immunogen delivery system complex defined in present Claim 1. In contrast to this, the relevant immunogen delivery system comprising at least one saponin and at least one sterol which forms part of the construct according to independent Claim 3 still embraces non-further characterized structures, e.g. of the Iscom type.

The use of immunogens for the preparation of formulations for transdermal delivery to be administered employing devices which comprise an occlusion vehicle within the meaning given in the present application has been previously disclosed. See, e.g. D1 (cf page 34, lines 11-25, Examples, Figs. 1-2 and Claims 1-12 and 24-25), D2 (cf "transdermal device" and "preparation of transdermal device" on pages 12-14, Examples 2-3 and Figs. 3A-3C) or D4 (cf page 30, lines 24-25; page 31, lines 32-33 bridging over page 32, lines 1-11 and Claim 52).

Thus, notwithstanding the observations on page 3, lines 19-28 of the application, it appears that the related prior art describes transdermal vaccination route approaches similar to those employed in the present disclosure (i.e. involving the use of an occlusion vehicle within the meaning given on page 9, lines 3-7) in which the skin is not treated (either by mechanical or chemical means) before application of the vaccine.

In the case of the transdermal devices for administration of an immunogen described in D2, an immunogen with or without an adjuvant is entrapped in a biphasic lipid vesicle which functions as delivery system of the immunogenic formulation of interest (see "transdermal device" and "preparation of the transdermal device" on pages 12-15). The transdermal device as shown e.g. in Fig. 3B of D2 comprises a backing layer (i.e. cover film) coated with a peripheral pressure sensitive adhesive and a reservoir for storage of a suspension of lipid vesicles to be administered transdermally (cf page 13, lines 22-29). The transdermal system of said Fig. 3B appears to be structurally and functionally analogous to the construct depicted in Figure 4 of the present application.

It is noted that the size of the lipid vesicles according to D2 is preferably of between 0.5 to 25 µm (cf page 10, lines 16-18) and that the results of Examples 3 and 7 substantiate a positive performance of the transdermal administration of vaccine formulations therein disclosed.

Attention is drawn to the characteristics of the patches for transcutaneous

immunization (i.e. immunization through the skin without penetration enhancement) employed in the immunization system described and claimed in D1 (e.g. page 6, lines 13-23; page 9, lines 25-33; page 10, lines 25-31 and Examples on pages 37-51). The immunogenic formulation applied to and/or incorporated in the pressure sensitive adhesive layer of the occlusion vehicle forming part of the transcutaneous delivery system of D1 preferably contains, in addition to the immunogen of interest, a protein with adjuvant activity (e.g. derived from an ADP-riboxylating exotoxin).

On the other hand, the desirable use of ISCOMS as delivery systems and/or adjuvants for the preparation of vaccine formulations is known from the related prior art (see e.g. D3). It is additionally noted that the cited D3 explicitly refers to the suitability of the therein described ISCOMS as adjuvants for transdermal administration of vaccines/antigenic compositions of interest (see page 7, lines 17-19).

In line with the above discussion it is not apparent on which grounds the construct defined in independent Claim 3, which still relies on the use of a non-further characterized immunogen delivery system comprising at least one saponin and at least one sterol (for instance of the ISCOM type), should be acknowledged as non-obvious to the person skilled in the administration of immunogenic preparations/adjuvanted vaccines. This objection (Art. 33(3) PCT) applies *mutatis mutandis* to the subject-matter of claims dependent/appended thereon, i.e. Claims 4-27 (part), 29-31(part) and 32-37(part).

2.4 Industrial applicability (Art. 33(4) PCT)

For the assessment of the present Claims 35-37 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

2.5 Further comments

(i) It appears that the meaning of the term "PosIntro" employed in the description and in present Claim 28 was not known before the date of priority of the present application. Furthermore, in contrast to the observations on page 4, lines 1-5 of the application, no reference to a "PosIntro" delivery system as such is to be found anywhere in the document WO 02/080981 (publication corresponding to the PCT/DK02/00229 referred to on page 4, lines 4-5). Instead of that, references to modified Iscoms may be found, for instance, on page 12, lines 13-19; page 14, lines 20-24; page 15, lines 9-13 or page 115, lines 28-29 of WO 02/080981.

Hence, the subject-matter for which protection is sought is open to interpretation in dependent Claim 28 and claims dependent/appended thereon (i.e. part of Claims 29-34 and 35-37), contrary to the clarity requirements of Art. 6 PCT

Insofar as the aforementioned document WO 02/080981 appears to be the first disclosure of the type of delivery systems hereby referred to as "PosIntro" it is considered that the definition of the preferred immunogen delivery system set forth in dependent Claim 29 as originally filed, should have been employed in Claim 28 in order to adequately characterize the delivery system corresponding to the arbitrary denomination "PosIntro".

(ii) There is no evidence in the application as originally filed to ascertain that in addition to immunogenic delivery systems of the "ISCOM" or "PosIntro" type (within the meaning given in the present application), any possible structural entity resulting from the interaction between sterols and saponins would be suitable to perform the transdermal delivery of at least one immunogen pursued in the claims. Therefore, the subject-matter of Claim 3 and claims dependent/appended thereon (i.e. part of Claims 4-27, 29-31, 32-34 and 35-37) is not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description and drawings.

The aforementioned lack of technical support in the description also results in the subject-matter encompassed by Claim 3 and part of Claims 4-27, 29-31, 32-34 and 35-37 being not sufficiently disclosed over the whole scope of the claims pursuant to Art. 5 PCT.

(iii) With respect to Claims 1, 9, 13, 20, 25, 26, 29 and 36 it is noted that the use of expressions like "preferably", "optionally", "such as" or "e.g." has no limiting effect on the scope of said claims, i.e. the feature(s) following such expressions is(are) to be regarded as entirely optional (cf PCT Guidelines, C-III, 4.6).

(iv) A corresponding publication number should have been given in the description when referring on page 28, line 26 to the PCT/DK02/00229 application (e.g. WO 02/080981).

(v) Apparently Claims 35-37 were meant to read "...wherein said individual is treated transdermally with a construct according to any of the claims 1 to 28."

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molecule size of about 1,5 – 2 nanometers, is reported to be very complicated to get to pass the skin membrane.

If a transdermal vaccination route could be provided, it would represent an important alternative to invasive administration, e.g. by way of intramuscular, intradermal or subcutaneous injections. Such injections present a range of disadvantages. They may cause stress, pain and irritation, particularly in the case of repeated injections, including the risk of infection - or may be poorly tolerated. Besides, untrained or unlicensed persons may not administer injections. Moreover, when applying for registration of a vaccine by the authorities, the required documentation of none adverse effects will obviously be more extensive for vaccines for invasive administration than for transdermal administration.

Vaccination in the present context is the process by which the application of a vaccine to an individual induces an immunological response in said individual under non-pathogenic conditions.

The transdermal vaccination route which has been described until now includes the steps wherein (i) the upper part of the skin, i.e. the stratum corneum, is removed by a mechanical treatment (scraped of) and (ii) the skin is moistened before application of the vaccine or alternatively (iii) the vaccine is absorbed in a gaze pad and applied on the skin with an ordinary plaster, these techniques is further described in e.g. Transcutaneous immunization, Glenn GM, Kenney RT. New Generation Vaccines, 3rd Ed. Vol. (in press) and in Advances in vaccine delivery: transcutaneous immunization, Glenn GM, Scharton-Kersten T, and Alving CR. Expert Opinion in Investigational Drugs. Vol. 8 (6) (1999): 797-805, WO 99/43350 and US 2001/0006645 A1.

It is an object of the present invention to provide novel compositions and a smarter, more simple and safe method for transdermal delivery under occlusion of an immunogen to an individual thereby avoiding the adverse effects connected with an invasive administration, such as injection.

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It is a further object of the invention to provide such compositions and methods, wherein the delivery is accomplished by the use of a delivery system, such as Posintro described in WO patent application no. PCT/DK02/00229 or ISCOMs as described in e.g. WO 98/36772, WO 92/06710 and WO 98/56420.

It has surprisingly been found that utilizing an occlusion vehicle and the principles according to the present invention can mediate an enhanced delivery of immunogen and can act as a potentiator of the immunogen to the immune active cells (often referred to as professional antigen presenting cells) subsiding beneath mucosal membranes, stratum corneum or beneath endothelia cell membranes. As the delivery system and/or adjuvant applied may assume a particulate shape with a mean size of about 5 to 50, e.g. most commonly between 10 and 40 nanometers (nm) or even larger, it is an unexpected observation that such relatively large particles are capable of demonstrating this enhancing feature. Based on observations regarding delivery of drugs, hormones and proteins it is generally anticipated that compounds larger than one or a few nanometers are incapable of penetrating the mentioned cellular membranes.

SUMMARY OF THE INVENTION

The present invention relates in a first aspect to a composition for transdermal delivery of at least one immunogen to an individual comprising

a) said at least one immunogen
b) an occlusion vehicle and
c) an immunogen delivery system in the form of a PosIntro or an ISCOM.

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reported to result in a variety of different structural entities, including entities such as e.g. lattices, honeycombes, rods, and amorphic particles, all of which structural entities are covered by the present invention.

In another embodiment the immunogen delivery system comprises a liposome. A liposome within the meaning of the present invention is generally spherical or spheroidal cluster or aggregate of amphipathic compounds, including lipophilic moieties, typically in the form of one or more concentric layers, for example, monolayers, bilayers or multi-layers. They may also be referred to herein as lipid vesicles. The liposomes may be formulated, for example, from ionic lipids and/or non-ionic lipids. Liposomes formulated from non-ionic lipids may be referred to as niosomes. Liposomes formulated, at least in part, from cationic lipids or anionic lipids may be referred to as cochleates.

The liposomes may be prepared e.g. as described by Lipford and Wagner (1994) in Vaccine, vol. 12, no. 1, p. 73-80, incorporated herein by reference. General liposomal preparatory techniques which may be adapted for use in the preparation of liposome compositions pertaining to the present invention are discussed, for example, in U.S. Pat. Nos. 4,728,578, 4,728,575, 4,737,323, 4,533,254, 4,162,282, 4,310,505, and 4,921,706; U.K. Patent Application GB 2193095A; International Application Serial Nos. PCT/US85/01161 and PCT/US89/05040; Mayer et al., Biochimica et Biophysica Acta, 858:161-168 (1986); Hope et al., Biochimica et Biophysica Acta, 812:55-65 (1985); Mayhew et al., Methods in Enzymology, 149:64-77 (1987); Mayhew et al., Biochimica et Biophysica Acta, 755:169-74 (1984); Cheng et al, Investigative Radiology, 22:47-55 (1987); and Liposome Technology, Gregoriadis, G., ed., Vol. I, pp. 29-31, 51-67 and 79-108 (CRC Press Inc., Boca Raton, Fla. 1984), the disclosures of each of which are hereby incorporated by reference herein.

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Accordingly, the liposome compositions may be prepared using any one of a variety of conventional liposomal preparatory techniques which will be apparent to one skilled in the art, including, for example, solvent dialysis, French press, extrusion (with or without freeze-thaw), reverse phase evaporation, simple freeze-thaw, sonication, chelate dialysis, homogenization, solvent infusion, microemulsification, spontaneous formation, solvent vaporization, solvent dialysis, French pressure cell technique, controlled detergent dialysis, and others, each involving the preparation of the compositions in various fashions. See, e.g., Madden et al., Chemistry and Physics of Lipids, 53:37-46 (1990), the disclosure of which is hereby incorporated herein by reference.

Suitable freeze-thaw techniques are described, for example, in WO application no. PCT/US89/05040, filed Nov. 8, 1989, the disclosure of which is hereby incorporated herein by reference in its entirety. Methods. which involve freeze-thaw techniques are preferred in connection with the preparation of liposomes. Preparation of the liposomes may be carried out in a solution, such as an aqueous saline solution, aqueous phosphate buffer solution, or sterile water. The liposomes may also be prepared by various processes which involve shaking or vortexing, which may be achieved, for example, by the use of a mechanical shaking device, such as a Wig-L-Bug.TM. (Crescent Dental, Lyons, Ill.), a Mixomat (Degussa AG Frankfurt, Germany), a Capmix (Espe Fabrik Pharmazeutischer Praeparate GMBH & Co., Seefeld, Oberay Germany), a Silamat Plus (Vivadent, Lechtenstein), or a Vibros (Quayle Dental, Sussex, England). Conventional microemulsification equipment, such as a Microfluidizer.TM. (Microfluidics, Woburn, Mass.) may also be used.

In one embodiment of the invention the immunogen delivery system comprises a biodegradable microsphere. In another embodiment the immunogen delivery system comprises an encapsulation system. In one

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Patent Claims

1. Composition for transdermal delivery of at least one immunogen to an individual comprising

a) said at least one immunogen
b) an occlusion vehicle and
c) an immunogen delivery system in the form of a PosIntro or an ISCOM.

2. Composition according to claim 1, wherein the occlusion vehicle is a pressure sensitive adhesive.

3. Composition for transdermal delivery of at least one immunogen to an individual comprising

a) said at least one immunogen
b) an occlusion vehicle in the form of a pressure sensitive adhesive and
c) an immunogen delivery system comprising at least one saponin and at least one sterol.

4. Composition according to any of the claims 1 to 3, wherein the transdermal delivery includes delivery through a skin surface or through a mucous membrane tissue.

5. Composition according to any of the claims 1 to 4, wherein the occlusion vehicle is a absorbing pressure sensitive adhesive.

6. Composition according to any of the claims 1 to 5, wherein the occlusion vehicle is a hydrocolloid adhesive.

7. Composition according to any of the claims 1 to 5, wherein the occlusion vehicle is a hydrogel adhesive.

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8. Composition according to any of the claims 1 to 5, wherein the occlusion vehicle is a cross-linked hydrogel adhesive.

9. Composition according to any of the claims 1 to 8, wherein the immunogen and the immunogen delivery system is distributed preferably homogenously in the occlusion vehicle.

10. Composition according to any of the claims 1 to 8, wherein the immunogen and the immunogen delivery system is distributed on the surface of the occlusion vehicle.

11. Composition according to claim 1, wherein the occlusion vehicle is a non-adherent occlusion vehicle, and further comprising a secondary adhesive, being separated from the vehicle, for skin fixation.

12. Composition according to claim 11, wherein the occlusion vehicle is dried or lyophilised and contains a carrier comprising a hydrophilic polymer substance or a grease like composition.

13. Composition according to any of the claims 1 to 12, wherein the occlusion vehicle or the secondary adhesive is a covering, such as a pad, a patch, a dressing or the like.

14. Composition according to any of the claims 12 or 13 further comprising a reservoir of water or other appropriate solvent/diluent.

15. Composition according to claim 14, wherein the water reservoir can be broken and the water or solvent/diluent can be absorbed in the occlusion vehicle.

16. Composition according to any of the claims 1 to 15 further comprising a rate controlling membrane.

17. Composition according to any of the claims 1 to 16, wherein the immunogen and/or the immunogen delivery system is separated from each other.

18. Composition according to any of the claims 1 to 17 further comprising an enhancer for transdermal drug delivery.

19. Composition according to any of the claims 1 to 18, wherein the at least one immunogen is selected in such a way that the induced immunological response is directed against one or more antigens.

20. Composition according to claim 19, wherein said one or more antigens are derived from a microorganism, preferably a pathogenic microorganism, such as a virus, a bacteria, a parasite and/or a fungus, or from a non-microbial organism, e.g. from an animal, such as a vertebrate.

21. Composition according to any of the claims 19 or 20, wherein the immunogen and/or antigen are derived from a virus.

22. Composition according to claim 21, wherein said one or more antigens are synthetic antigens, antigens derived from said individual or antigens derived from any species.

23. Composition according to any of the claims 19 or 20, wherein said induced immunological response confers protection in said individual against a pathogenic microorganism which said antigen or antigens are part of.

24. Composition according to any of the claims 19-20 or 23, wherein said induced immunological response may act upon subsequent exposure of the individual to said pathogenic microorganism.

25. Composition according to any of the claims 19-20 or 23-24, wherein said induced immunological response is directed against a pathogenic component

produced by said pathogenic microorganism during infection of said individual, e.g. bacterial toxins, such as tetanus toxin.

26. Composition according to any of the claims 1 to 25, wherein the immunogen and/or antigen comprise or consist of

i) one or more identical or different polypeptides and/or peptides, which polypeptides and/or peptides optionally comprise posttranslational modifications,
ii) one or more identical or different lipopeptides, such as polypeptides and/or peptides chemically linked to a lipid group,
iii) one or more identical or different nucleic acid sequence or sequences, which may encode polypeptides and/or peptides, or
iv) one or more identical or different polysaccharides and/or oligosaccharides,

or combinations thereof, and wherein the immunogen and/or antigen may further be processed into fragments.

27. Composition according to any of the claims 1 to 26, wherein the immunogen and the immunogen delivery system is comprised within a vaccine formulation.

28. Composition according to claim 3, wherein the immunogen delivery system is a PosIntro or an ISCOM.

29. Composition according to any of the claims 1 to 28, wherein the immunogen delivery system is a complex comprising:

i) at least one first sterol and/or at least one second sterol,

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wherein the at least one second sterol is capable of contacting a foreign antigen, preferably a nucleic acid by means of an interaction selected from an electrostatic interaction and a hydrophobic interaction, and
wherein the at least one first sterol and/or the at least one second sterol is capable of forming a complex with at least one first saponin and/or at least one second saponin, and

ii) at least one first saponin and/or at least one second saponin,

wherein the at least one second saponin is capable of contacting a genetic determinant by means of an interaction selected from an electrostatic interaction and a hydrophobic interaction, and
wherein the at least one first saponin and/or the at least one second saponin is capable of forming a complex with at least one first sterol and/or at least one second sterol, and optionally

iii) at least one contacting group for contacting a genetic determinant by means of an interaction selected from an electrostatic interaction and a hydrophobic interaction,

with the proviso that the at least one contacting group is present when no second sterol is present in the complex and further optionally

iv) at least one lipophilic moiety.

30. Process for the preparation of a composition according to any of the claims 1 to 29, comprising the steps of introducing the immunogen and the immunogen delivery system, which are optionally comprised within a vaccine formulation, into the matrix of the occlusion vehicle or on its surface by dispersion or soaking in a solution of the vehicle or by applying to its surface,

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and optionally sterilising and/or drying and/or seal packaging the composition.

31. Process according to claim 30 further comprising the step of drying or lyophilisation or the immunogen and the immunogen delivery system before introducing into the vehicle.

32. Process according to any of the claims 30 or 31 further comprising the step of adding one or more enhancers for transdermal drug delivery and/or one or more plasticizers.

33. Construct comprising a composition according to any of the claims 1 to 29.

34. Construct according to claim 33, having one or more compartments.

35. Construct according to any of the claims 33 or 34 having at least two compartments, wherein a first compartment comprises a lyophilised pad comprising the immunogen and the immunogen delivery system and a second compartment comprises water or other appropriate solvent/diluent.

36. Construct according to any of the claims 33 to 35 comprising at least two separate components.

37. Method for generating an immunological response in an individual wherein a composition according to any of the claims 1 to 29 is administered to said individual.

38. Method for treating or preventing a condition of illness in an individual, e.g. a disease caused by infection of said individual by a pathogenic microorganism, wherein a composition according to any of the claims 1 to 29 is administered to said individual.

39. Method for vaccination of an individual wherein a composition according to any of the claims 1 to 29 is administered to said individual.

40. Use of an immunogen for the preparation of a composition for transdermal delivery of said immunogen comprising an occlusion vehicle.